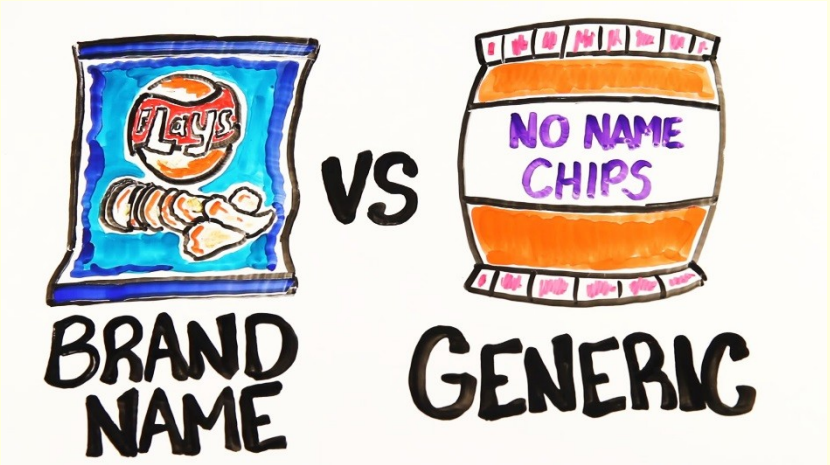
Pharmacodynamics

Wesam El Bakly,
Assistant Professor of Pharmacology,
Medicine, ASU

Drug Nomenclature



Drug Nomenclature

1. Chemical:

-long name, refers to the chemical structure of the drug

2. Generic:

-shorter preferred name, derived from the chemical name

-Official or approved name

3. Trade-brand name:

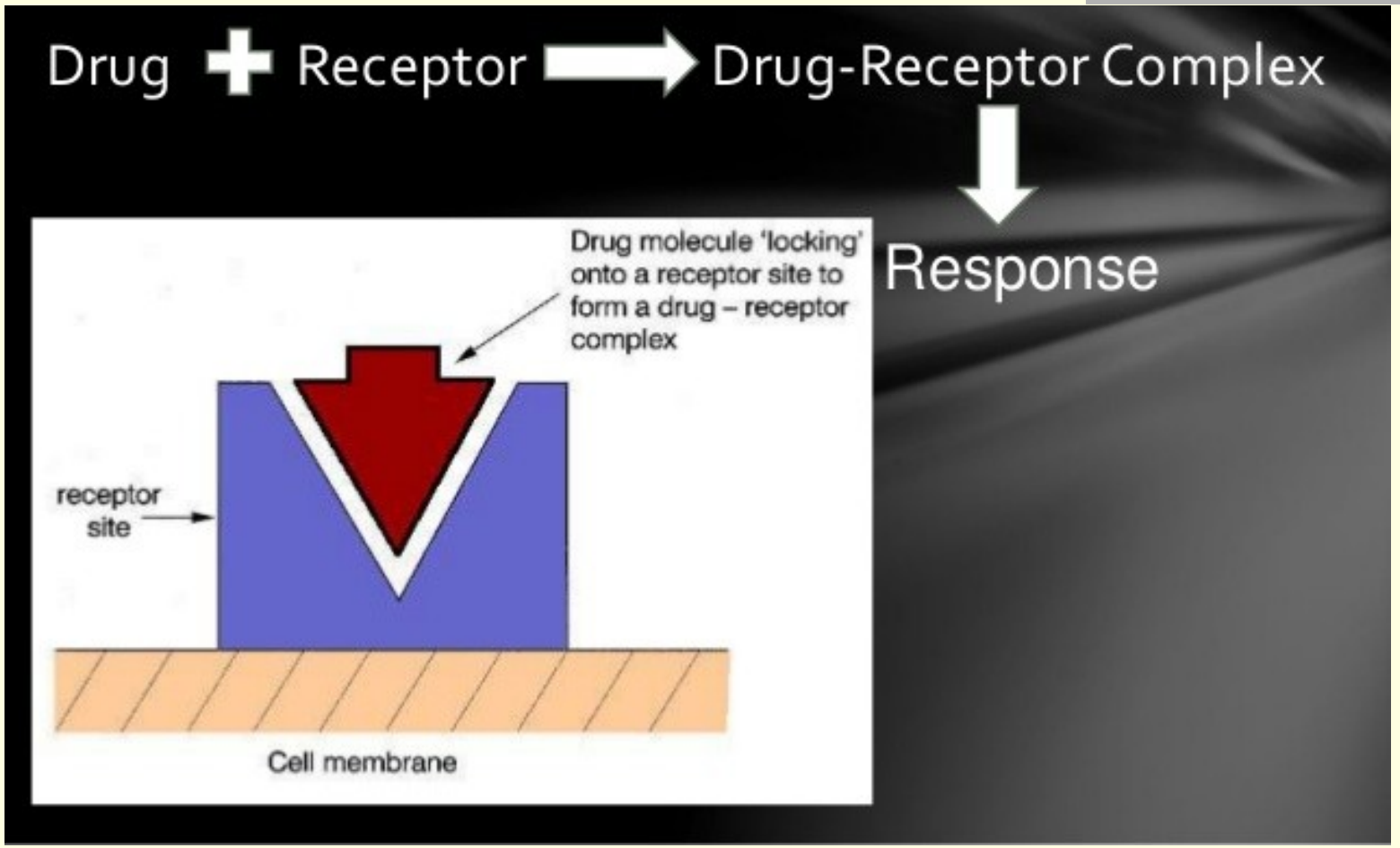
- assigned by the manufacturer

Generic versus brand?

Generic drugs are copies of brand-name drugs that have exactly the same dosage, intended use, effects, side effects.

Brand Name	Generic
Tylenol	paracetamol
Valium	Diazepam

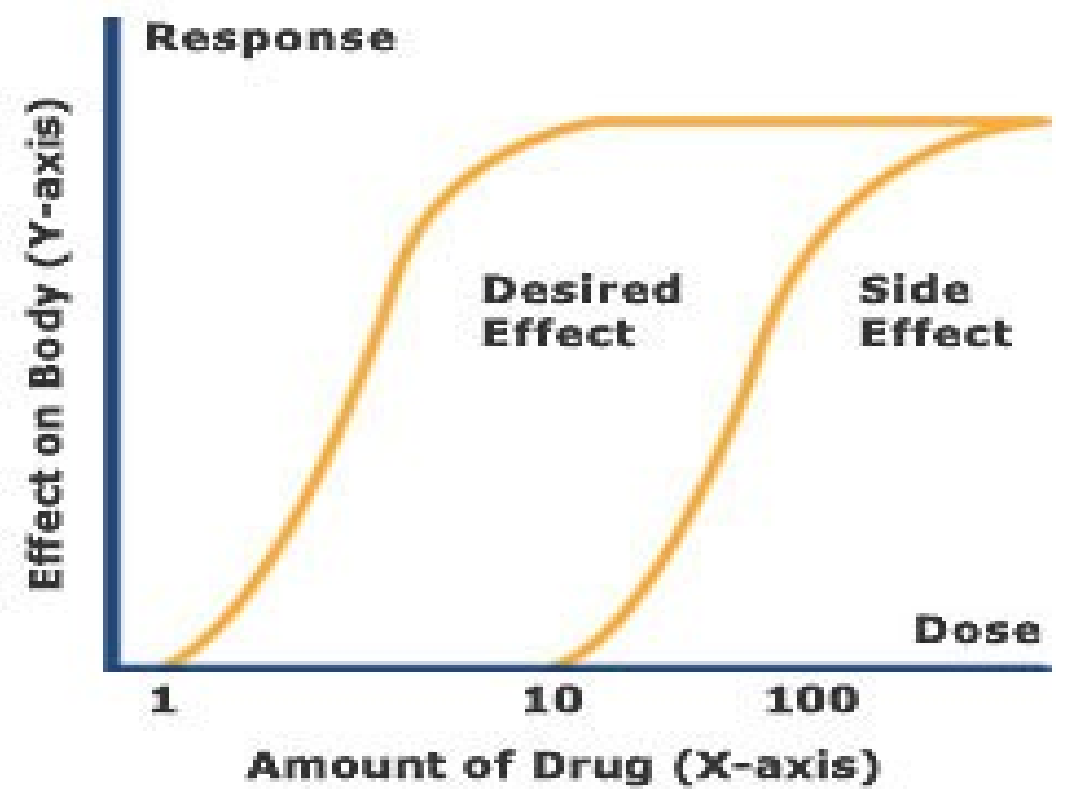
How drug response is obtained?

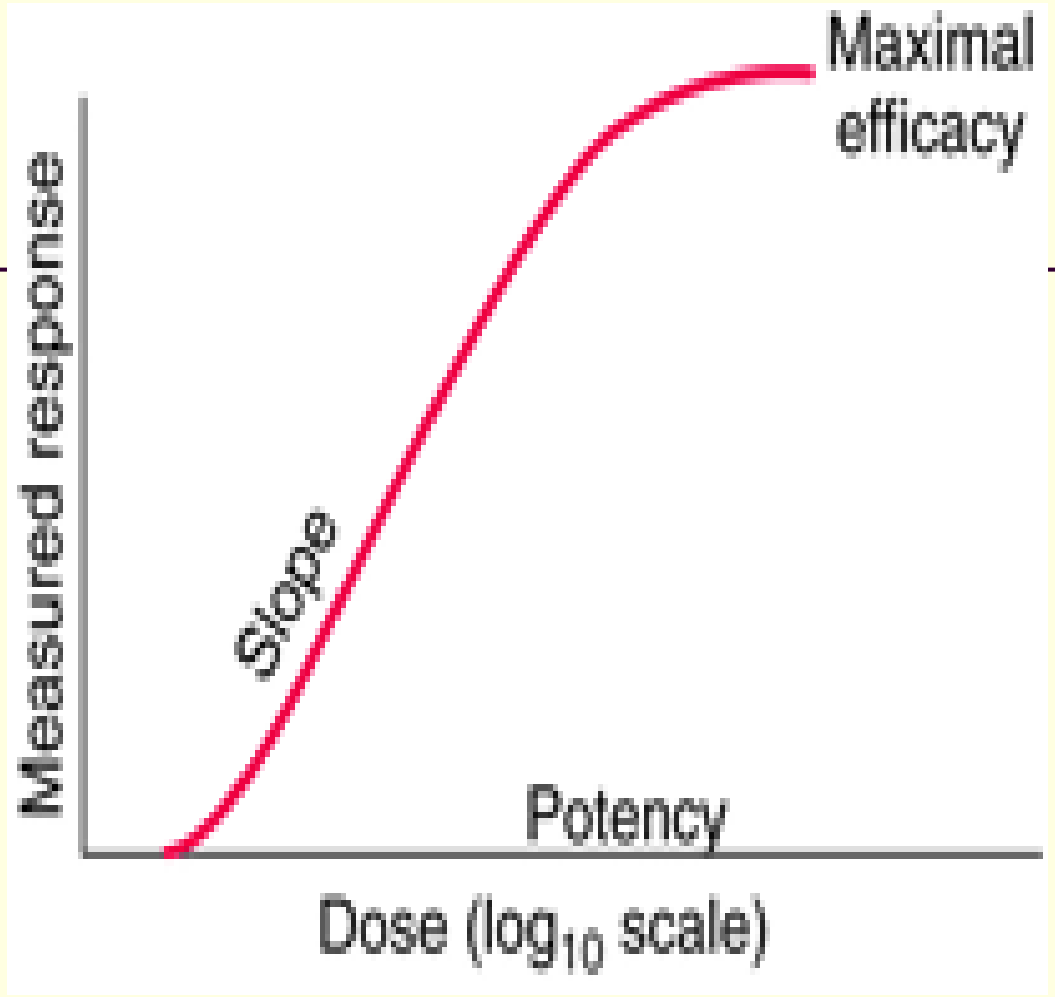


Relation between drug dose & clinical response

Dose Response Curve

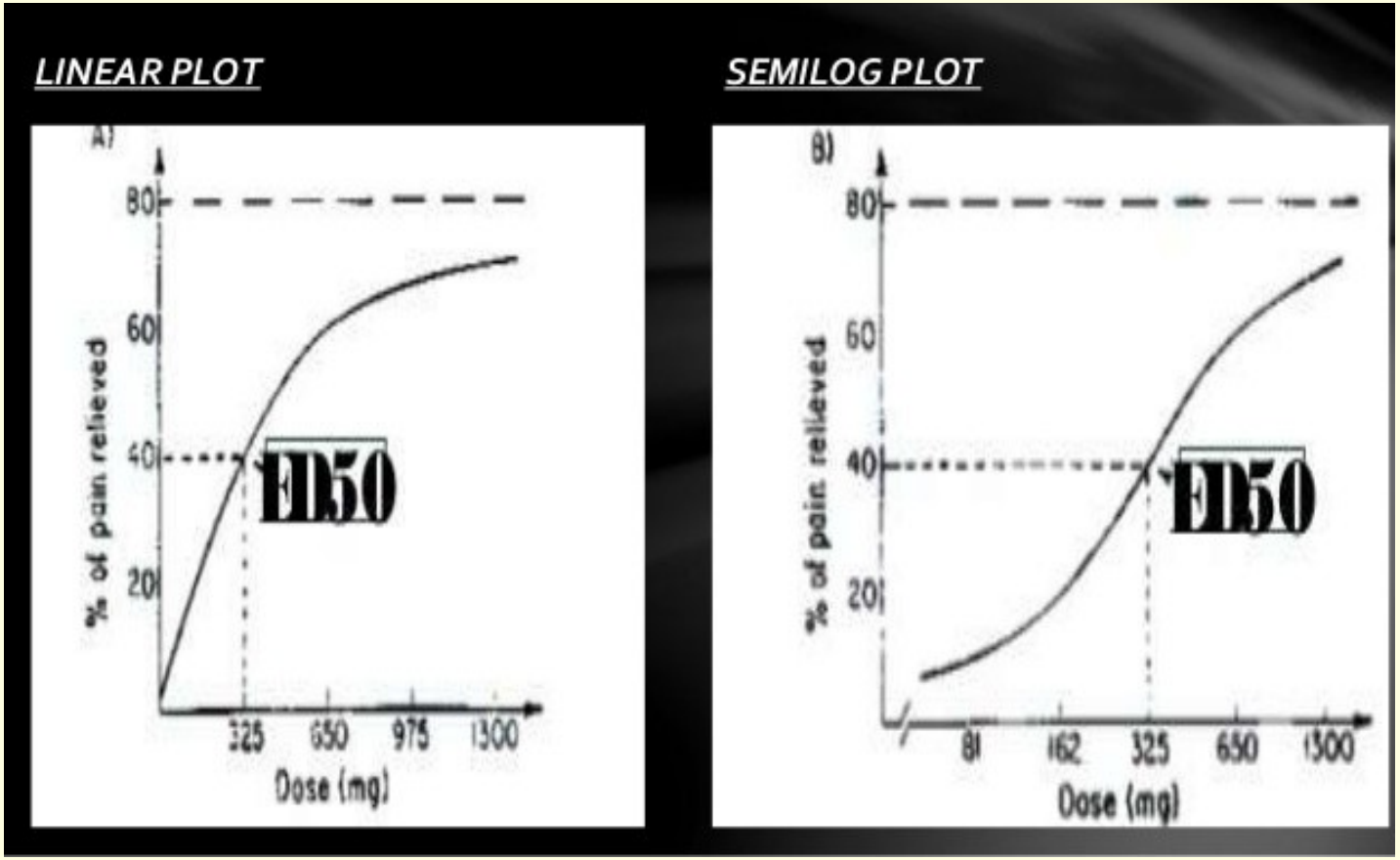
Dose-response curves determine how much of a drug (X-axis) causes a particular effect, or a side effect, in the body (Y-axis).





Dose-response curve.

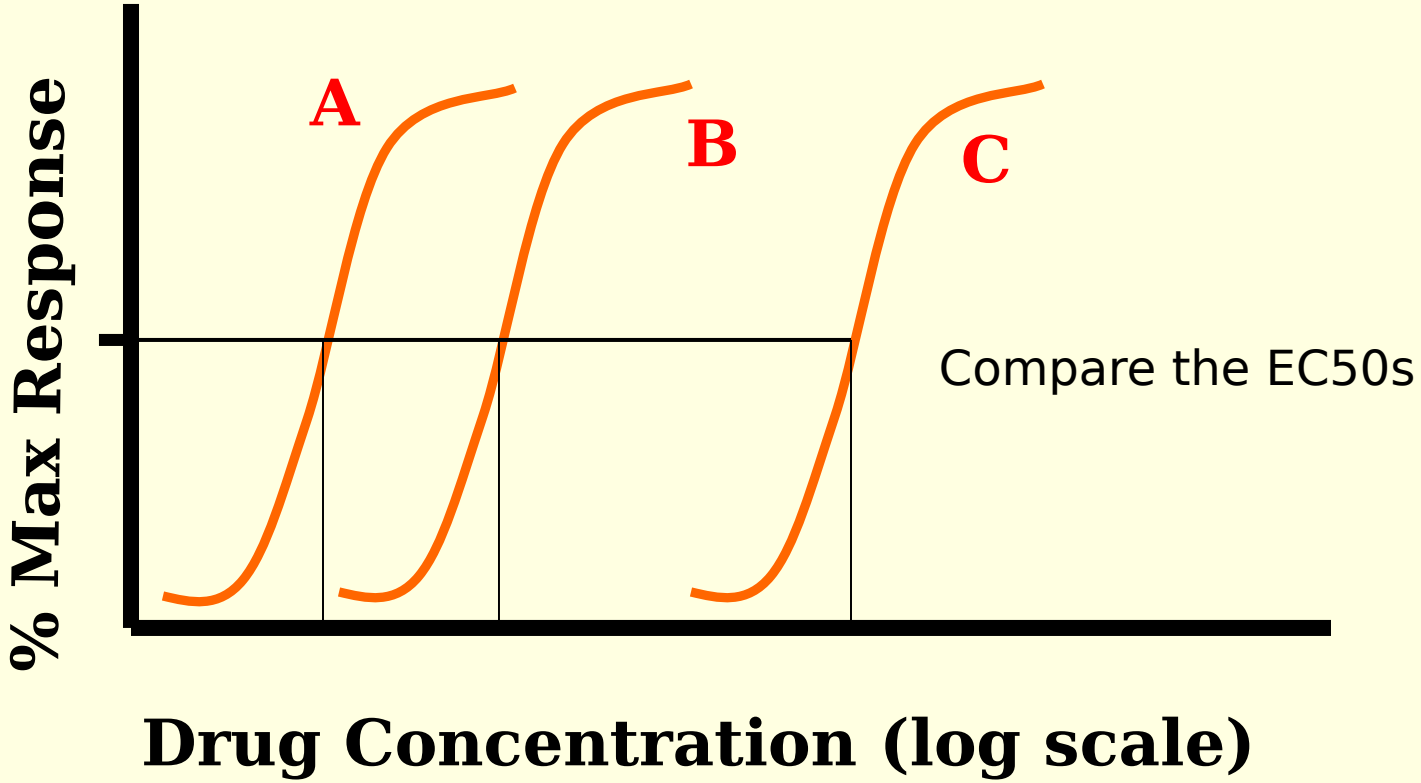
Dose response curve studying the effect of aspirin

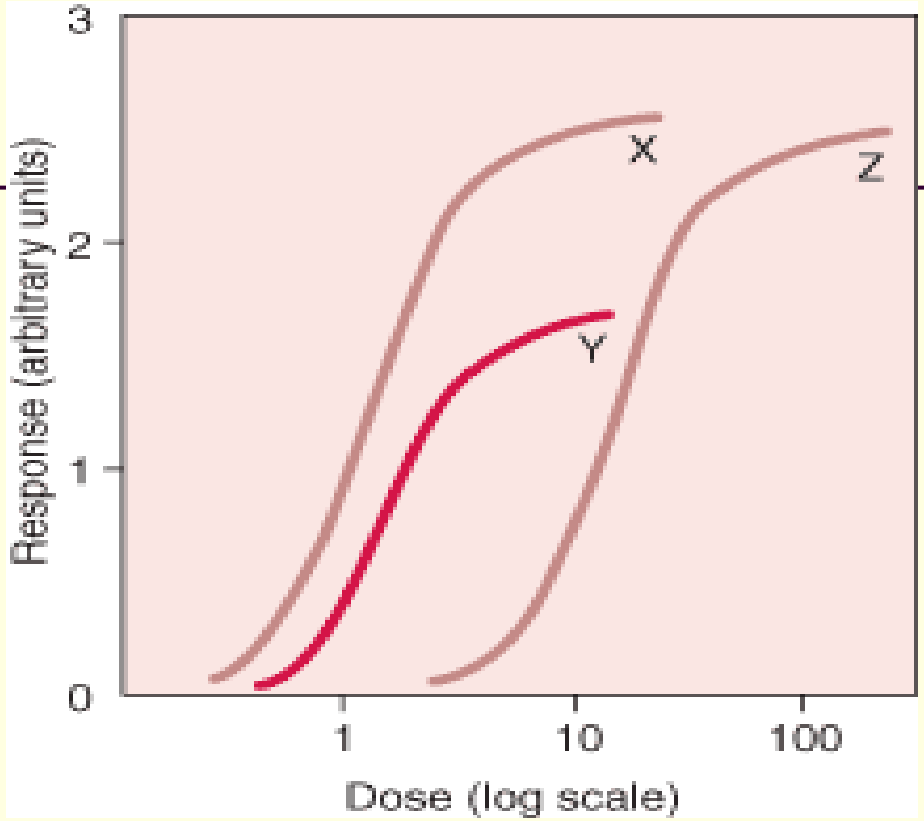


Parameters can be obtained from Dose response curve

- Efficacy: the maximal effect of a drug
  - Morphine is more effective than aspirin
  - Emax
- Potency: the amount of drug that produce a desired response
  - E.g. analgesic dose of morphine 10mg, pethidine 100mg (??? More potent)
  - ED50

Full Agonists (i.e., equal efficacies) that Differ In Potency:



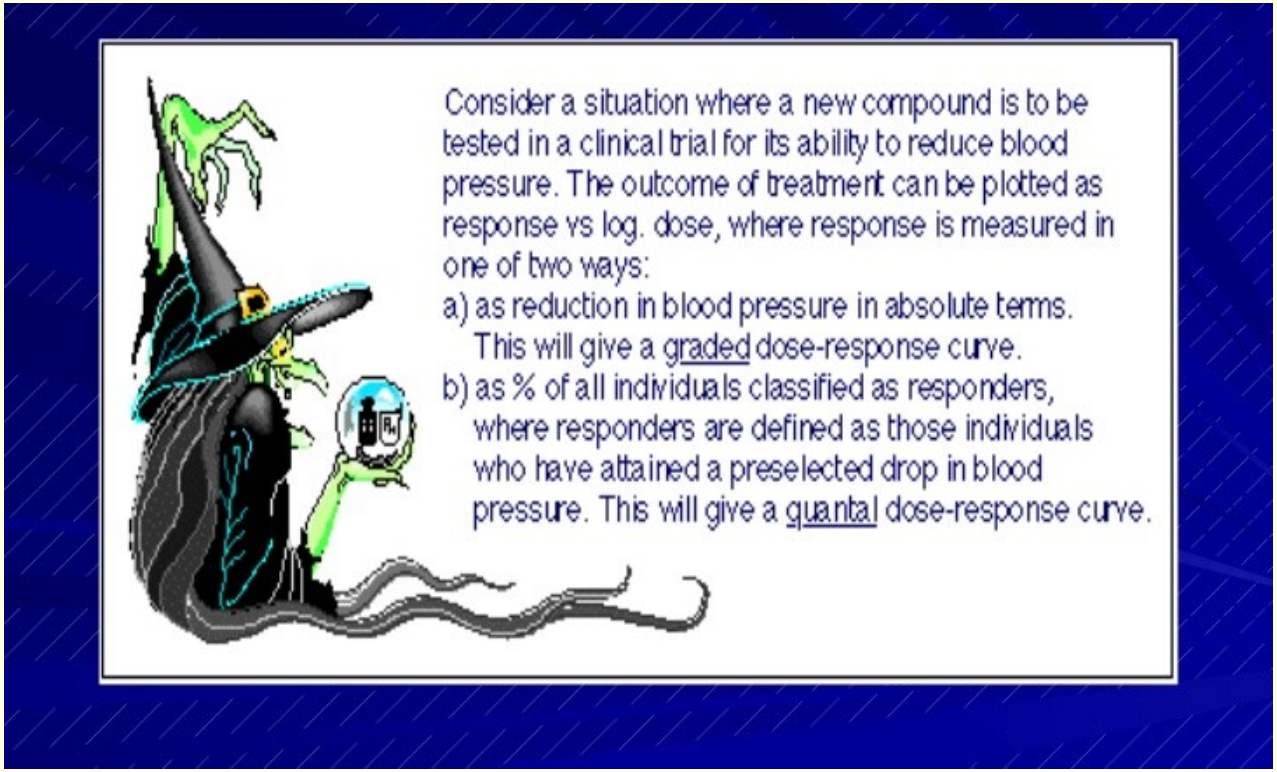


- **Drug X more potent than drug Y or Z.**
- **Drugs X and Z have equal efficacy, indicated by their maximal attainable response (ceiling effect).**
- **Drug Y is more potent than drug Z, but its maximal efficacy is lower.**

Types od dose response curve

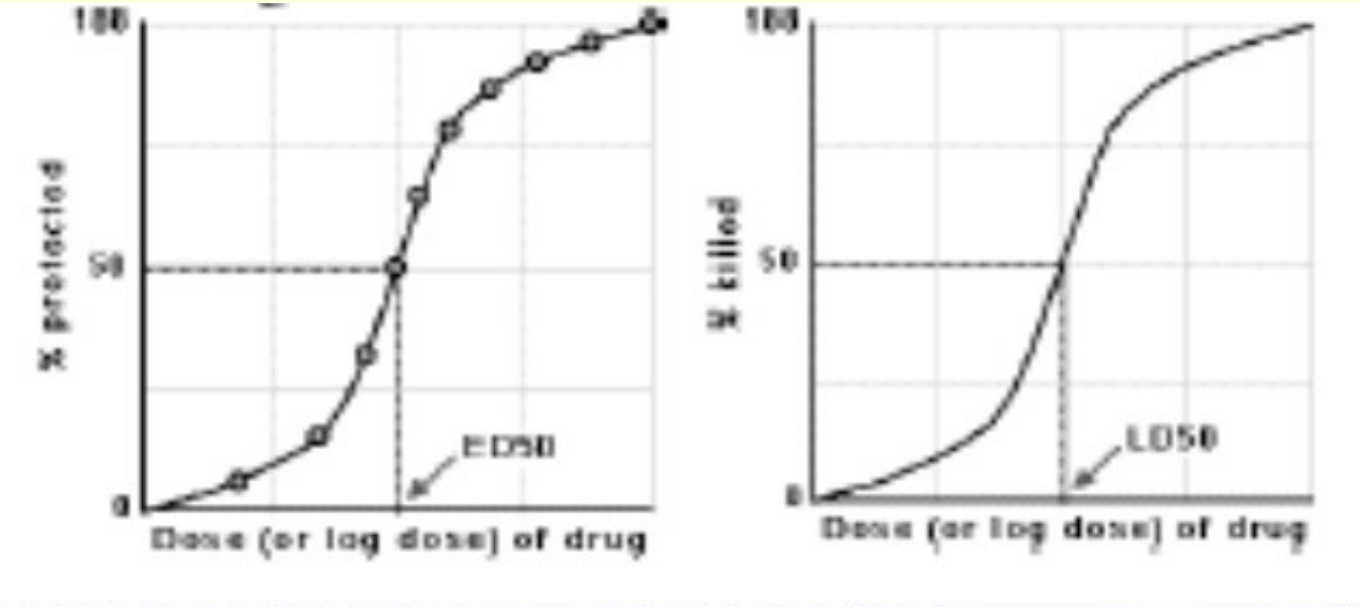
- Graded dose response curve
- All/None dose response curve

What is the difference between Graded and all or none curve?



All/none dose response curve

Y axis: all or none effect (alive or dead. Asleep or awake, in pain or pain free)
On Y axis, you plot percentage of population showing an effect as a function of a dose



Parameters from All/None dose response curve

- ED50
- LD50
- Therapeutic index

The lower LD50 the more toxic the drug
The higher TI the safer the drug

Signaling mechanism & mechanism of drug action

Mechanism of drug action

- Receptor mediated
- Non-receptor mediated

Non-receptor mediated Mechanism

- Enzyme (CHEIs, aspirin)
- Chelation (desferrioxamine)
- Physical means
  - Demulcent (bismuth salts)
  - Adsorbents (charcoal)
  - Lubricants (liquid paraffin)
- Chemical means: antacid

Types of receptors

Cellular protein that interact with a ligand to produce a response

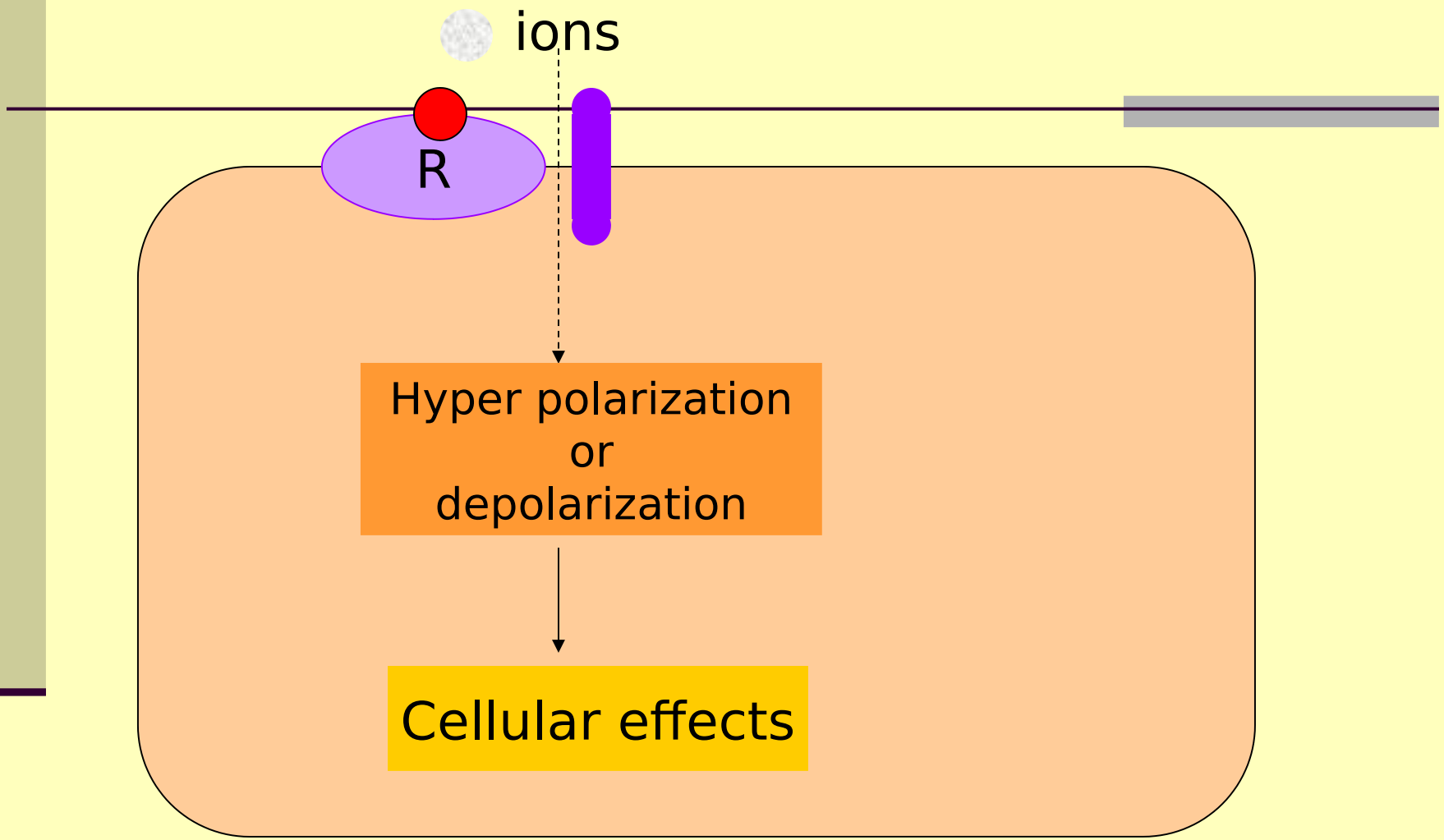
- Ligand gated ion channels
- G protein coupled receptors
- Receptor linked to Tyrosine Kinases
- Intracellular receptors regulating transcription

Ligand gated ion channel (iontropic receptors)

- Nicotinic acetylcholine receptors

Onset of action is the fastest

Ligand gated ion channel (iontropic receptors

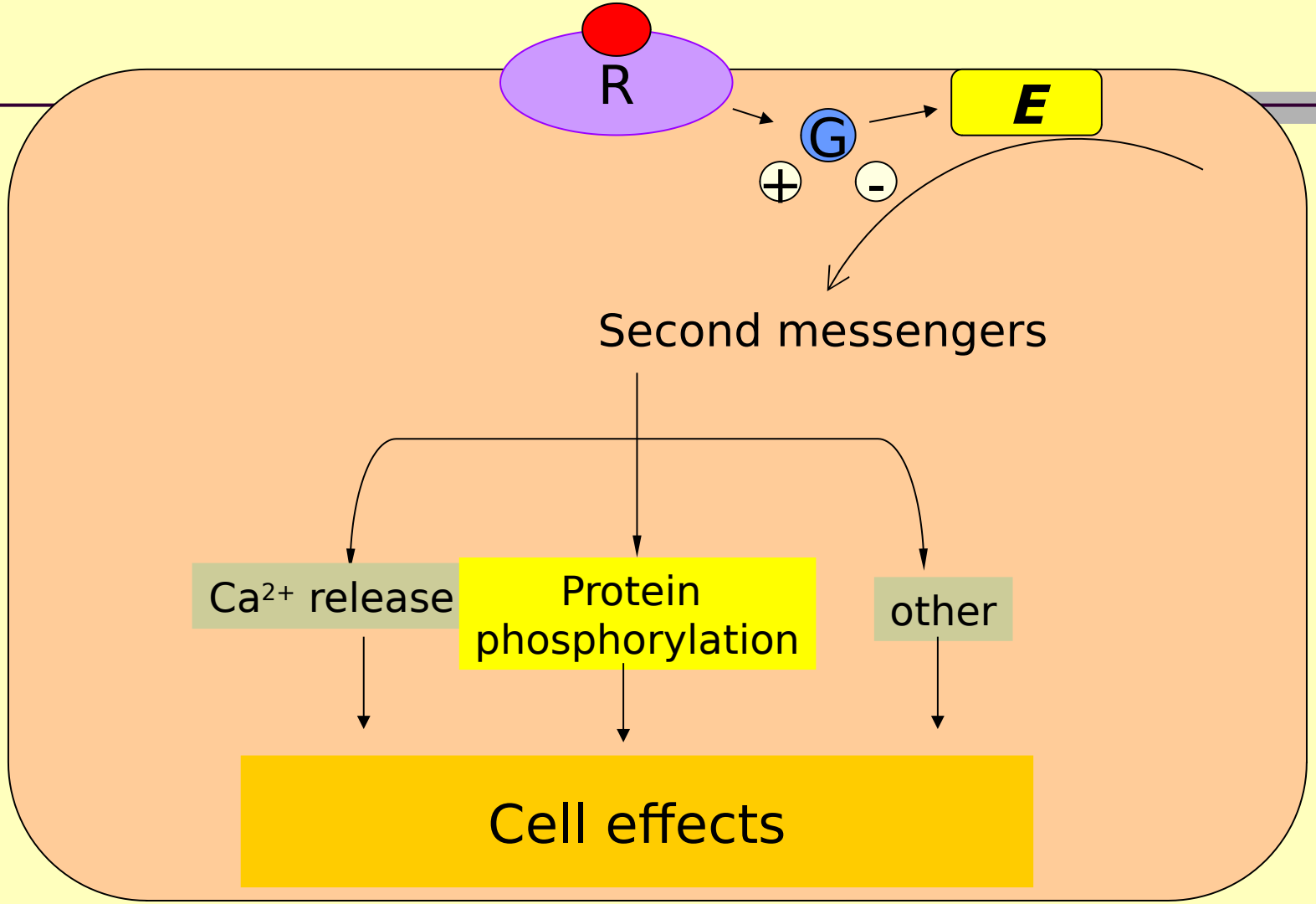


G protein coupled receptors

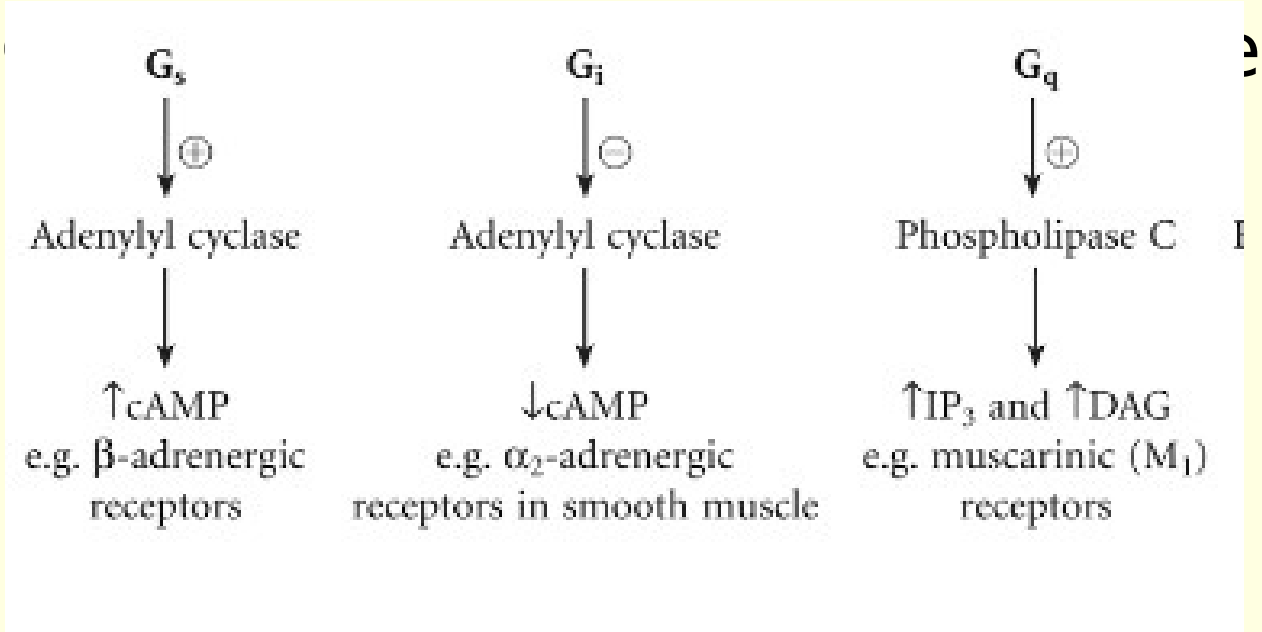
- Muscarininc Acetylcholine
- Catecholamines (α and β)

Onset: slow

G protein coupled receptors

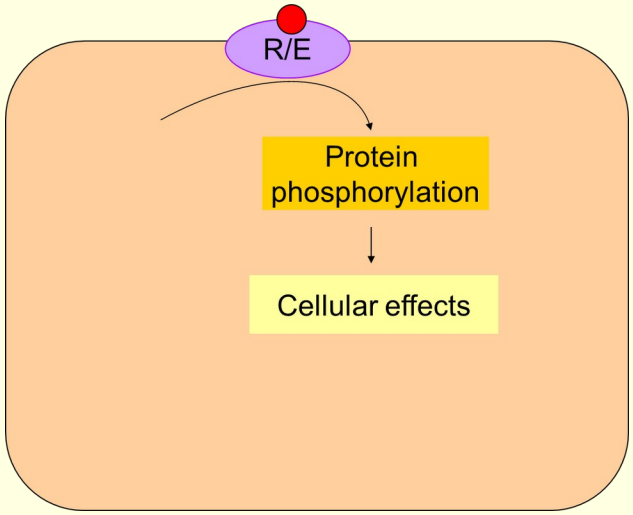


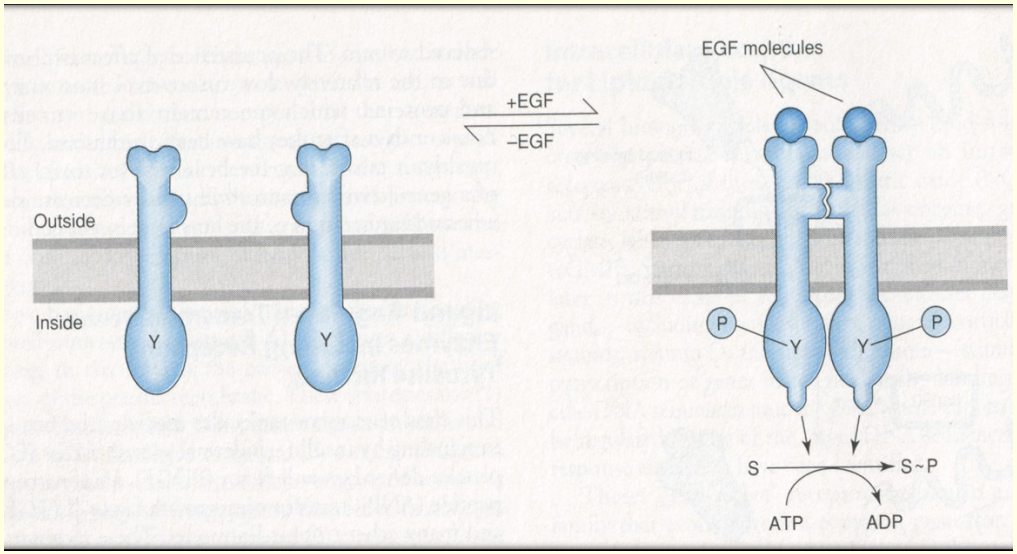
Well Established Second Messengers

- Cyclic Adenosine Monophosphate (cAMP)
- Phosphoinositides (IP3)
- 

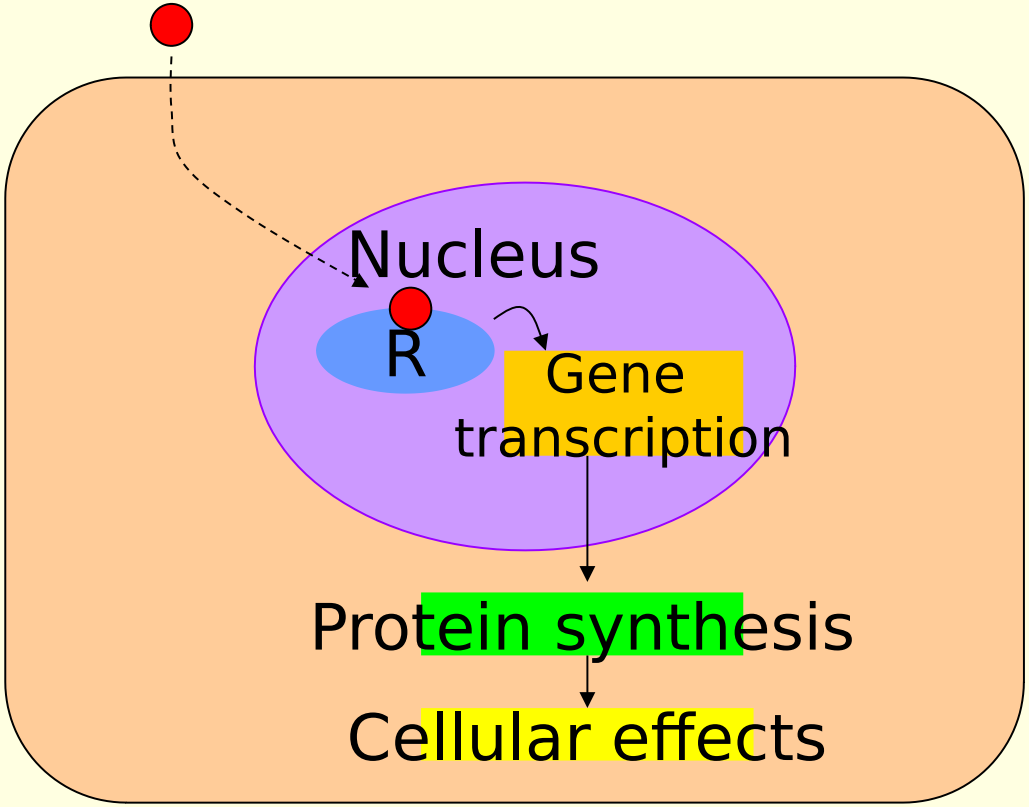
Receptors linked to tyrosine Kinase

insulin





Intracellular receptors



Examples:
thyroid hs,
vitamin D,
steroid

Very sloww

Receptor cycling or turnover

Table 1.6 Regulation of Receptors

Receptor Downregulation	Receptor Upregulation
Prolonged use of agonists ↓ ↓↓ Receptor number and sensitivity ↓ ↓↓ Drug effect For example, chronic use of salbutamol downregulates β_2-adrenoceptors, which may be responsible for decreased effect of salbutamol in asthmatics.	Prolonged use of antagonists ↓ ↑↑ Receptor number and sensitivity On sudden stoppage of the antagonist ↓ ↑↑ Response to agonist For example, when propranolol is stopped after prolonged use, some patients experience withdrawal symptoms, such as nervousness, anxiety, palpitation, tachycardia, rise in BP, increased incidence of angina or even MI may be precipitated. This is due to upregulation or supersensitivity of β-adrenoceptors to catecholamines. Therefore, propranolol should not be discontinued abruptly.

Tolerance

- Reduced response to the drug on repeated administration
- So higher doses are required to produce the same effect

Why?

PK causes

PD causes

Tachyphylaxis

- Acute tolerance but the same effect cannot be obtained by increase the dose
- e.g. amphetamine

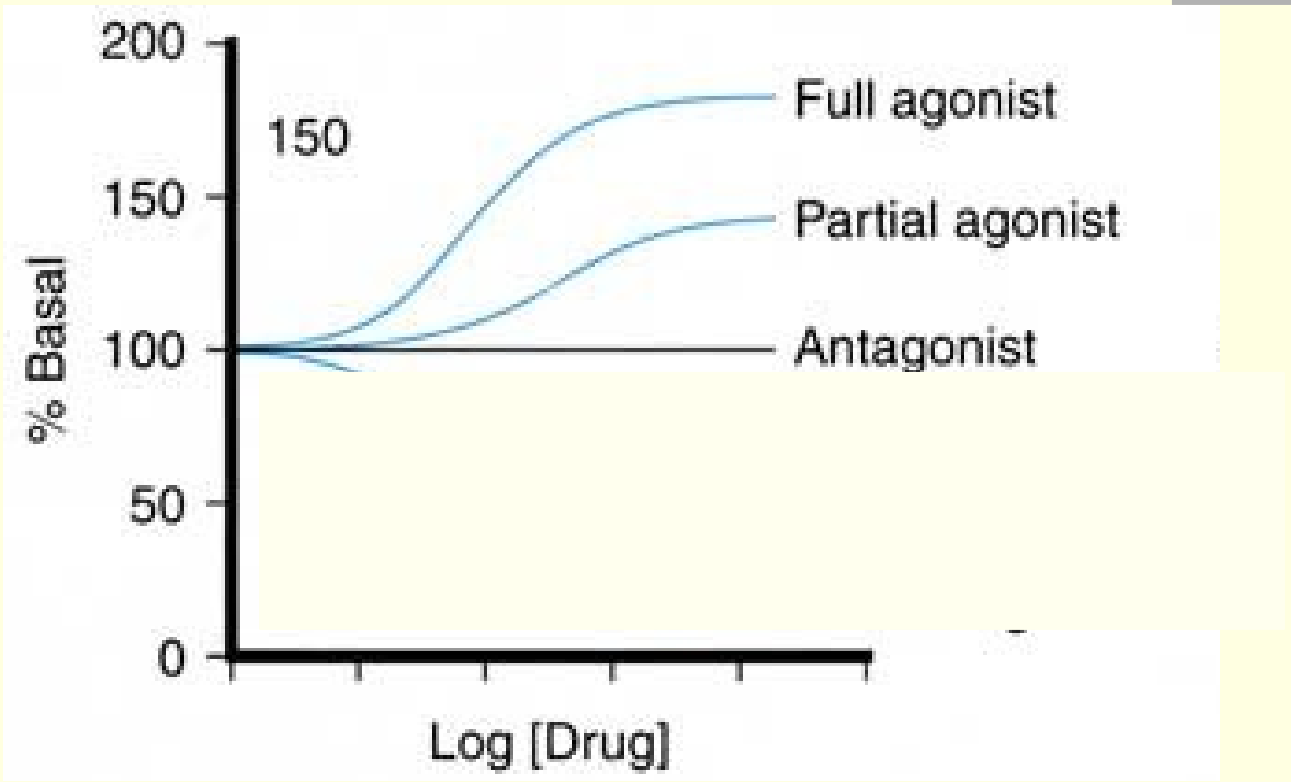
Cross tolerance

- Tolerance to related drugs (opioids)

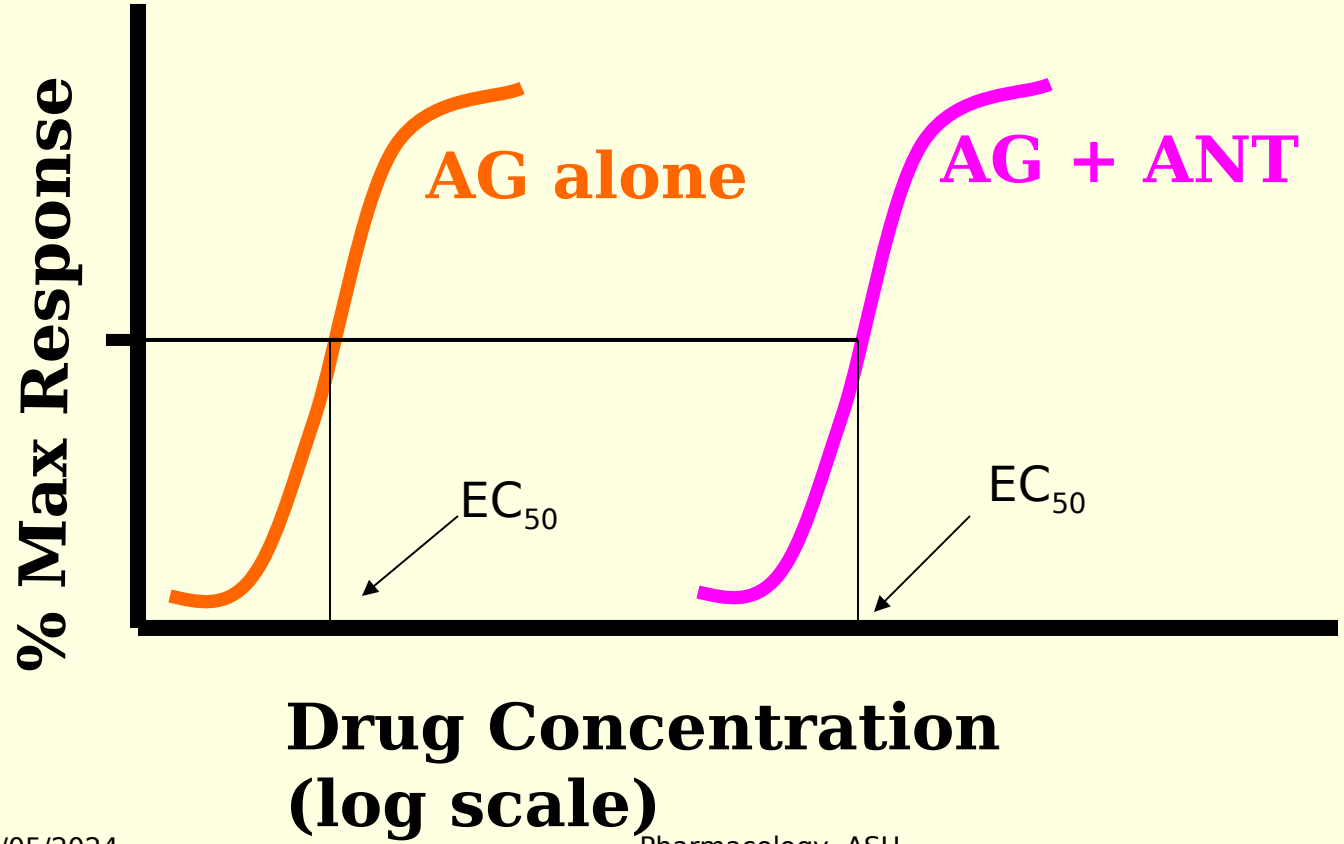
Agonists and Antagonists

- **AGONIST** - Has affinity for receptor and efficacy.
- **ANTAGONIST** - Has affinity but no efficacy.
- **Partial Agonist** or Partial Antagonist –
  - Has affinity but *lower* efficacy than full agonist.
  - e.g. succinylcholine

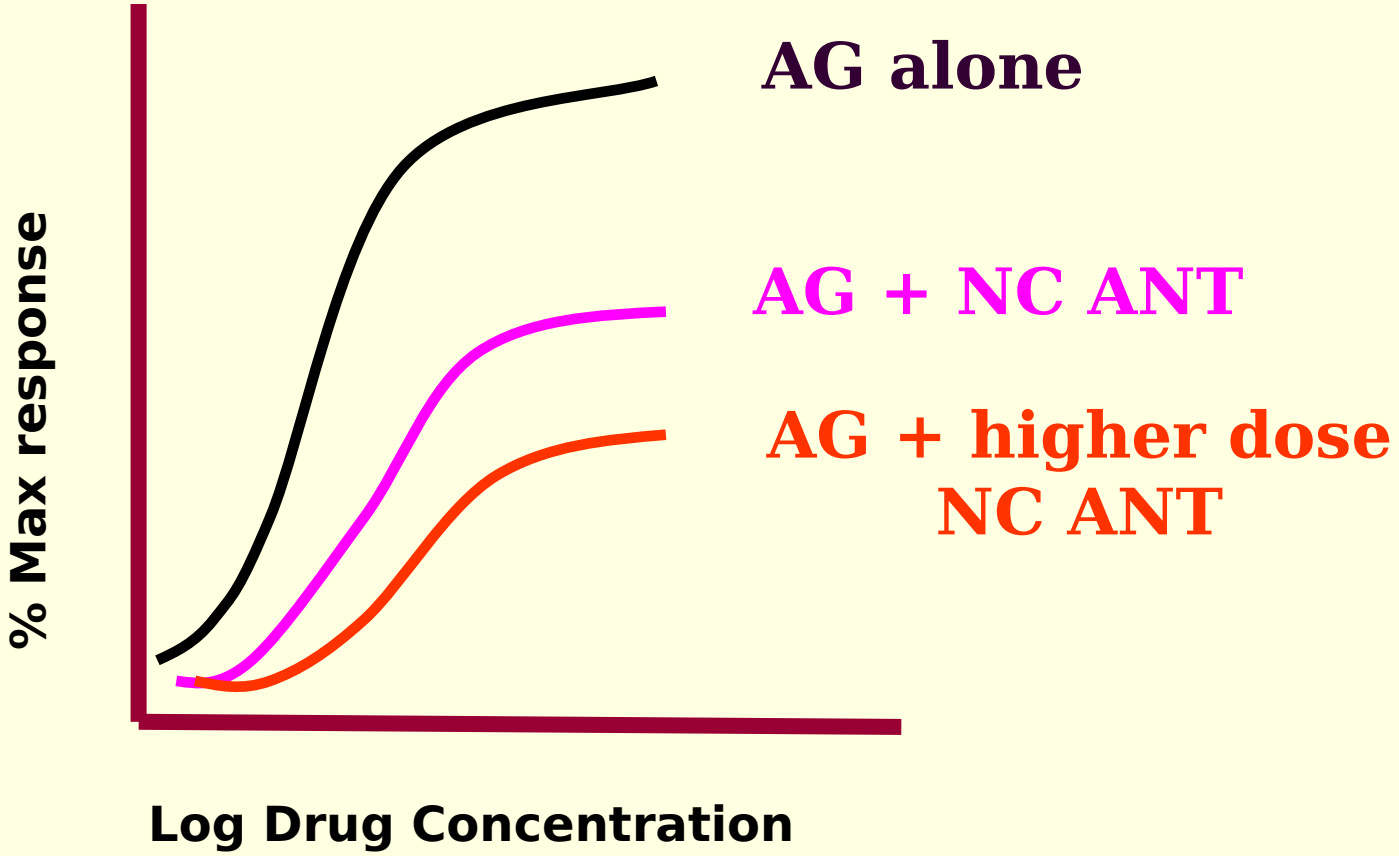
Receptor ligand types



Competitive Antagonism Shifts The Agonist D-R Curve (*Potency*)

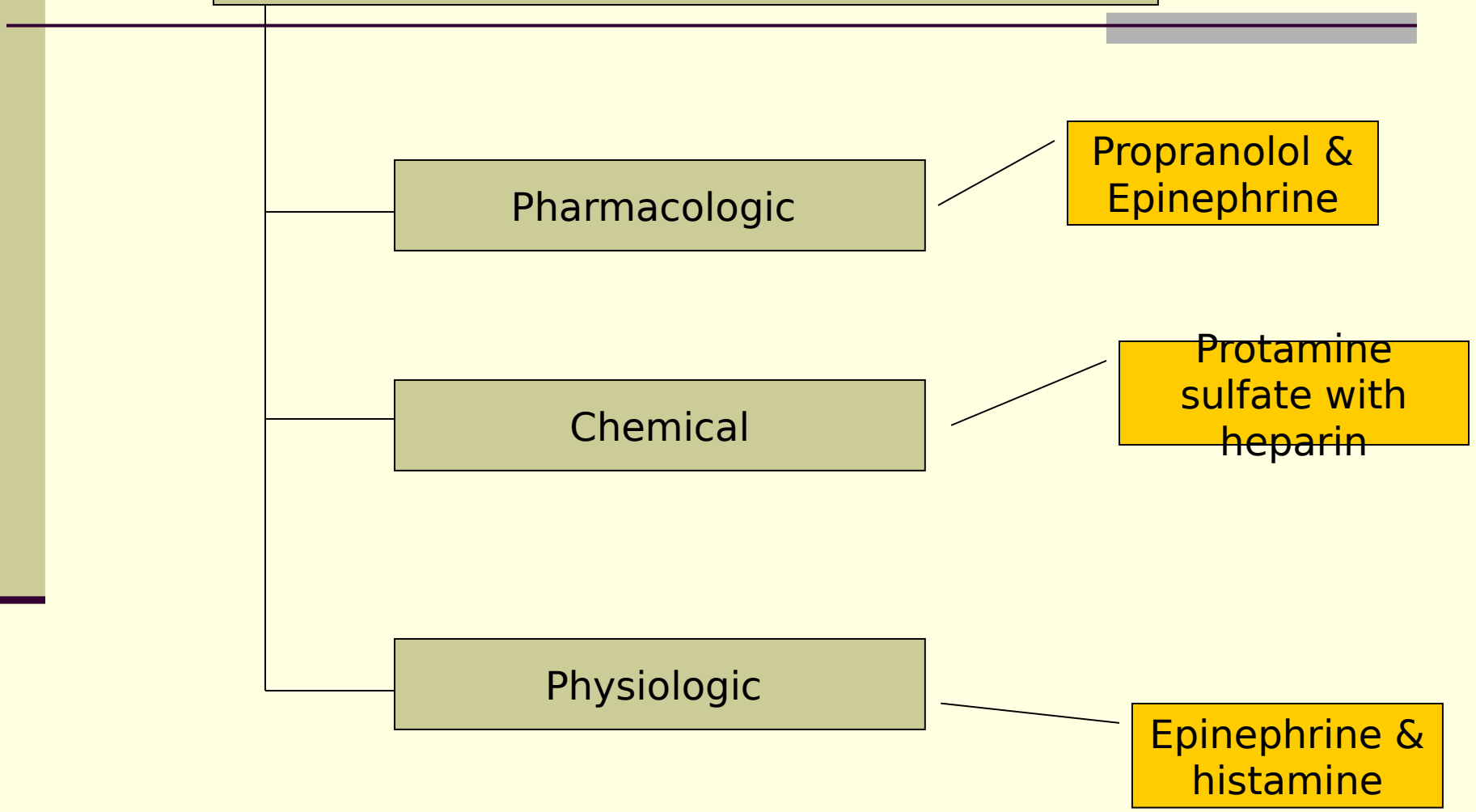


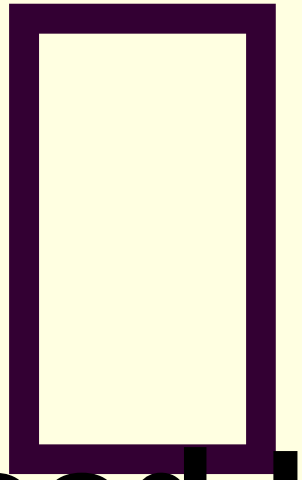
Noncompetitive Antagonism Decreases Agonist *Efficacy*



Competitive versus non competitive antagonist

Drug Antagonism





Good Luck